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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/898,238	WACKETT ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *7-10 and 24-27*.

   Claim(s) withdrawn from consideration: *17 and 18*.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit: 1652

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments filed in the Paper of 12/1/2003, have been fully considered and are deemed not to be persuasive to overcome the rejections previously applied. Claims 7-10, 17, 18, and 24-27 are at issue and are present for examination.
Claims 17 and 18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 9 and 24-27 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an atrazine chlorohydrolase that comprises an amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any atrazine chlorohydrolase that comprises an amino acid sequence having greater than about 80% sequence identity to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
The rejection is stated in the previous office action as it applies to claims 9 and 24-27.
Applicants comments regarding those statements made at page 6 that "the currently named genus encompasses not only an amino acid substitution here or there but the mutation of almost 100 amino acids or a fifth of the total amino acids of the disclosed protein." are acknowleged.
Applicants continue to traverse this rejection on the basis that the reference to the specification as lacking the establishment: (A) regions of the protein structure which may be modified without effecting atrazine chlorohydrolase activity; (B) the general tolerance of atrazine chlorohydrolases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a atrazine chlorohydrolase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficien guidance as to which of the essentially infinite possible choices is likely to be successful, is a requirement not made necessary by the statute and applicants are unaware of case law as such. Applicants are reminded that the statute does require guidance to make and us the claimed genus , and those points illustrated by (A) through (D) each are means of providing such guidance, which the instant application does not provide. Applicants are reminded that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
While methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., having atrazine chlorohydrolase activity) requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification.
Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain atrazine chlorohydrolase activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable
Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any atrazine chlorohydrolase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 7, 9, 10, and 24-27 remain rejected under 35 U.S.C. 102(a) as being anticipated by Mandelbaum et al. (Applied and Environmental Microbiology, Vol 61, No. 4, pages 1451-1457, Apr. 1995, See IDS) as evidenced by DeSouza et al. (Journal of Bacteriology, Vol 178, No. 16, pages 4894-4900, Aug. 1996).
The rejection was stated in the previous office action.
Applicants continue to traverse this rejection on the basis that Mandelbaum et al. do not teach each element of the claim, specifically applicants emphasize that the previous interpretation of "isolated and purified" based on applicants specification, page 8, lines 22-25, as in vitro isolation of a DNA or protein from its natural cellular environment" was incomplete and taken out of context. Applicants continue to argue that the definition of "isolated and purified" plainly precludes further isolation which would be necessary so that an "isolated and purified" protein can be sequenced . Applicants point to the recitation "so that it can be sequenced..." as proof that the definition plainly precludes such further isolation. Applicants further submit that if the previous assertions made by the examiner are correct, then "an AtzA protein in a cell extract would be considered isolated." And applicants suggest that they have addressed this issue at page 19, line 21 which states "AtzA protein can be isolated from cell extracts." And thus the specification explicitly states that an AtzA present in a cell extract cannot be considered to be isolated. Applicants argument continues to be found nonpersuasive. First applicants are reminded that proteins can be "isolated and purified" to varying degrees and that the terms isolated and purified as used in applicants claims and specification and as discussed in this and previous office actions does not preclude the "isolated and purified AtzA protein" taught by Mandelbaum et al. While it is admitted that the protein taught by Mandelbaum et al. may not be "isolated and purified" to the extent as that by applicants, it remains that it is "isolated and purified". Second while one of skill in the art would further isolate and purify the protein taught by Mandelbaum et al. prior to sequencing the protein, it remains that the protein taught by Masndelbaum et al. in its taught "isolated and purified state" can be sequenced, albeit after further purification.
Thus claims 7, 9, 10, and 24-27 remain anticipated by Mandelbaum et al. as evidenced by DeSouza et al.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mandelbaum et al. (Applied and Environmental Microbiology, Vol 61, No. 4, pages 1451-1457, Apr. 1995, See IDS) and Kennedy (See IDS).
The rejection is stated in the previous office action.
Applicants arguments and response mailed on November 26, 2002 are again noted. With respect to applicants comments regarding the dependency of claim 8 on claim 7 are acknowledged, however applicants are reminded that claim 7 is anticipated by Mandelbaum et al. above, and anticipation is the pinnacle of obviousness.